

Application No. 10/609,120

Attorney Docket No. 11187-00016

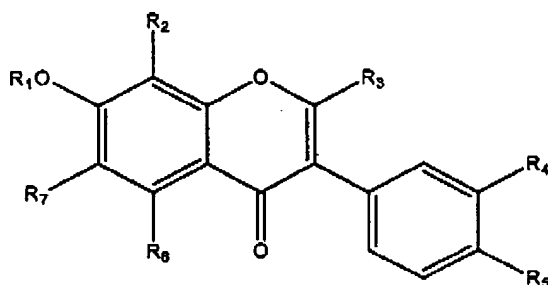
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Reply to Office Action of May 11, 2005

LISTING OF THE CLAIMS

The following listing of claims will replace all prior versions and listing of claims in the application. It is noted that no amendments to the claims have been made herein.

1. (Previously Presented) A method for inhibiting ALDH-2 comprising contacting ALDH-2 with a compound of Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, and heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

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R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, carboxy and sugar;

R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

R<sub>5</sub> is selected from the group consisting of hydrogen, carboxy, hydroxy, amino, halo, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy carbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxy carbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy carbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

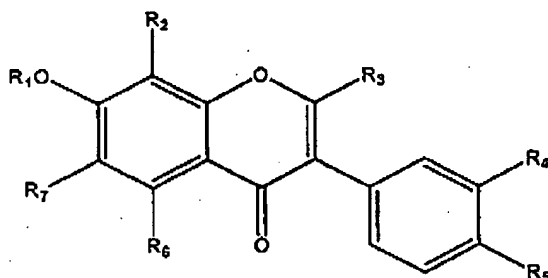
R<sub>7</sub> is selected from the group consisting of hydrogen and halogen

with the proviso that R<sub>5</sub> cannot be hydroxy when R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>6</sub>, and R<sub>7</sub> are all hydrogen.

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2. (Previously Presented) A method for inhibiting ALDH-2 comprising contacting ALDH-2 with a compound of Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, (C<sub>5</sub>-C<sub>10</sub>)carboxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocycliloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkoxycarbonyl, carboxy and sugar;

R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

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R<sub>3</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

R<sub>7</sub> is selected from the group consisting of hydrogen, halogen, and C<sub>1</sub>-C<sub>6</sub> alkoxy.

3. (Previously Presented) The method of claim 1, wherein R<sub>5</sub> is hydroxy or amino.
4. (Original) The method of claim 2, wherein R<sub>1</sub> is a straight chain alkyl.
5. (Previously Presented) The method of claim 2, wherein R<sub>1</sub> is (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl or (C<sub>5</sub>-C<sub>10</sub>)carboxyalkyl.
6. (Original) The method of claim 1, wherein the ALDH-2 is human ALDH-2.

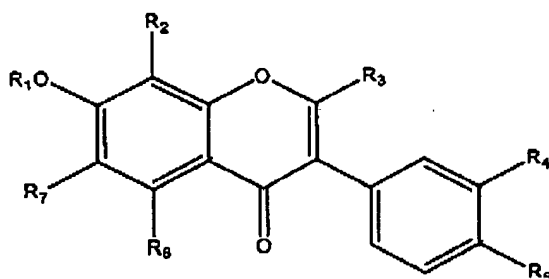
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7. (Previously Presented) A method of modulating alcohol consumption in a mammal comprising administering a compound of Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, and heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

R<sub>3</sub> is selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkoxycarbonyl, carboxy and sugar;

R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

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R<sub>5</sub> is selected from the group consisting of hydrogen, carboxy, hydroxy, amino, halo, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

R<sub>7</sub> is selected from the group consisting of hydrogen and halogen,

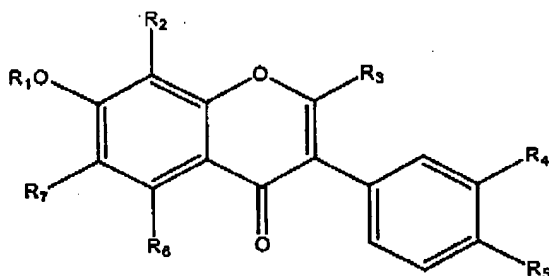
with the proviso that R<sub>5</sub> cannot be hydroxy when R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>6</sub>, and R<sub>7</sub> are all hydrogen

in an amount effective to increase a concentration of an aldehyde formed during catabolism of a neurotransmitter.

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8. (Previously Presented) A method of modulating alcohol consumption in a mammal comprising administering a compound of Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, (C<sub>5</sub>-C<sub>10</sub>)carboxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclioxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

R<sub>3</sub> is selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, carboxy and sugar;

R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

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R<sub>5</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

R<sub>7</sub> is selected from the group consisting of hydrogen, halogen, and C<sub>1</sub>-C<sub>6</sub> alkoxy,

in an amount effective to increase a concentration of an aldehyde formed during catabolism of a neurotransmitter.

9. (Original) The method of claim 7, wherein the mammal is a human.
10. (Original) The method of claim 7, wherein the neurotransmitter is serotonin or dopamine.
11. (Original) The method of claim 7, wherein the aldehyde is 5-hydroxyindoleacetaldehyde or 3,4-dihydroxyphenylacetaldehyde.



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(Endow-3)

Reply to Office Action of May 11, 2005

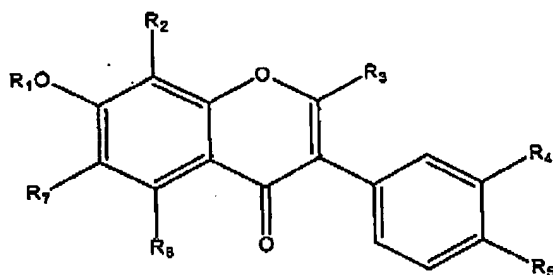
12. (Original) The method of claim 7, wherein the compound does not inhibit monoamine oxidase.
13. (Currently Amended) The method of claim 7, wherein  $R_5$  is hydroxy or amino.
14. (Original) The method of claim 8, wherein  $R_1$  is a straight chain alkyl.
15. (Original) The method of claim 8, wherein  $R_1$  is  $(C_1C_6)$ hydroxyalkyl or  $(C_5-C_{10})$ carboxyalkyl.
16. (Original) The method of claim 7, wherein the compound is administered intraperitoneally, intramuscularly or orally.

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17. (Previously Presented) A method for identifying a compound that modulates ALDH-2 comprising the steps of:

i) providing a compound of Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, and heterocycloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

R<sub>3</sub> is selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>6</sub>) alkoxycarbonyl, carboxy and sugar;

R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

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R<sub>5</sub> is selected from the group consisting of hydrogen, carboxy, hydroxy, amino, halo, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

R<sub>7</sub> is selected from the group consisting of hydrogen and halogen, ;

with the proviso that R<sub>5</sub> cannot be hydroxy when R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>6</sub>, and R<sub>7</sub> are all hydrogen

- ii) contacting ALDH-2 with the compound;
- iii) assaying the ability of the compound to modulate ALDH-2 activity; and
- iv) selecting a compound that modulates ALDH-2 activity as a modulator of ALDH-2 activity.

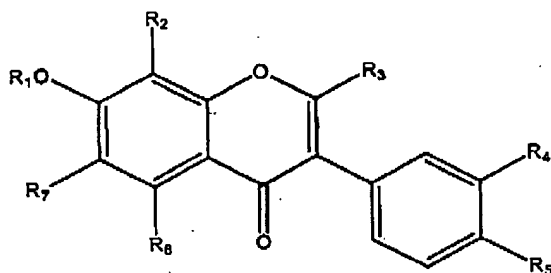
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18. (Previously Presented) A method for identifying a compound that modulates ALDH-2 comprising the steps of:

- i) providing a compound of Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, (C<sub>5</sub>-C<sub>10</sub>)carboxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

R<sub>3</sub> is selected from the group consisting of hydrogen C<sub>1</sub>-C<sub>6</sub> alkoxycarbonyl, carboxy and sugar;

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R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

R<sub>5</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocycliloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di(C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

R<sub>7</sub> is selected from the group consisting of hydrogen, halogen, and C<sub>1</sub>-C<sub>6</sub> alkoxy;

- ii) contacting ALDH-2 with the compound;
- iii) assaying the ability of the compound to modulate ALDH-2 activity; and
- iv) selecting a compound that modulates ALDH-2 activity as a modulator of ALDH-2 activity.

19. (Original) The method of claim 17, wherein the modulation is inhibition.

20. (Original) The method of claim 17, wherein the compound is further capable of increasing a concentration of an aldehyde.

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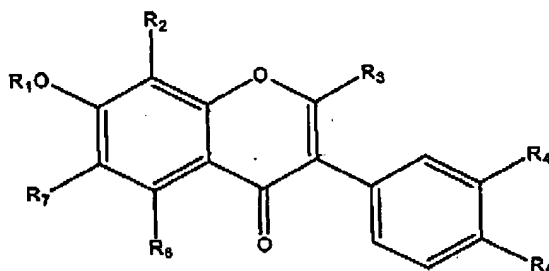
21. (Original) The method of claim 20, wherein the aldehyde is 5-hydroxyindoleacetaldehyde or 3,4-dihydroxyphenylacetaldehyde.
22. (Original) The method of claim 17, wherein the compound does not inhibit monoamine oxidase.
23. (Previously Presented) The method of claim 17, wherein R<sub>3</sub> is hydroxy or amino.
24. (Original) The method of claim 18, wherein R<sub>1</sub> is a straight chain alkyl.
25. (Previously Presented) The method of claim 18, wherein R<sub>1</sub> is (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl or (C<sub>5</sub>-C<sub>10</sub>)carboxyalkyl.

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26. (Previously Presented) A compound for inhibiting ALDH-2 comprising Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, and heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

R<sub>3</sub> is hydrogen;

R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

R<sub>5</sub> is selected from the group consisting of hydrogen, carboxy, hydroxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-

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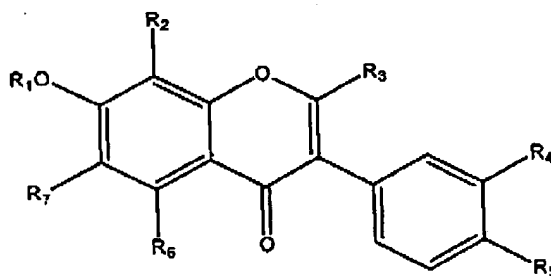
C<sub>6</sub>cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

R<sub>7</sub> is selected from the group consisting of hydrogen and halogen,

with the proviso that R<sub>5</sub> cannot be hydroxy when R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>6</sub>, and R<sub>7</sub> are all hydrogen.

27. (Previously Presented) A compound for inhibiting ALDH-2 comprising Formula I



Formula I

wherein:

R<sub>1</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-



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C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, (C<sub>5</sub>-C<sub>10</sub>)carboxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl;

R<sub>2</sub> is selected from the group consisting of hydrogen and alkoxy;

R<sub>3</sub> is hydrogen;

R<sub>4</sub> is selected from the group consisting of hydrogen and hydroxy;

R<sub>5</sub> is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)haloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkadienyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, (C<sub>3</sub>-C<sub>6</sub>)cyclohaloalkoxy, (C<sub>2</sub>-C<sub>6</sub>)alkynyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkoxyalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)alkylcarbonyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkylcarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>4</sub>-C<sub>6</sub>)alkoxycarbonylalkyl, (C<sub>1</sub>-C<sub>6</sub>)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, (C<sub>1</sub>-C<sub>3</sub>)alkylamino, di(C<sub>1</sub>-C<sub>3</sub>)alkylamino, (C<sub>1</sub>-C<sub>2</sub>)alkoxy(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, di(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>1</sub>-C<sub>2</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylcarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl, and di (C<sub>1</sub>-C<sub>3</sub>)alkylaminocarbonyl

R<sub>6</sub> is selected from the group consisting of hydrogen and hydroxy; and

R<sub>7</sub> is selected from the group consisting of hydrogen, halogen, and C<sub>1</sub>-C<sub>6</sub> alkoxy.

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(Endow-3)

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28. (Previously Presented) The compound of claim 26, wherein  $R_5$  is hydroxyor amino.
29. (Original) The compound of claim 27, wherein  $R_1$  is a straight chain alkyl.
30. (Previously Presented) The compound of claim 27, wherein  $R_1$  is ( $C_1$ - $C_6$ )hydroxyalkyl or ( $C_5$ - $C_{10}$ )carboxyalkyl.
31. (Original) The compound of claim 26, wherein the compound further inhibits alcohol consumption in a mammal.
32. (Original) The compound of claim 31, wherein the mammal is a human.